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Letter to the Editor

Hemoglobin ≤ 12.9 g/dl predicts risk of antibiotic treatment in cystic fibrosis

I read with interest the letter by Kathiresan et al. [1] reporting their observations of statistically-significant increases in hemoglobin concentration during 156 consecutive admissions of cystic fibrosis (CF) patients for the treatment of infective exacerbation with parenteral antibiotics. These authors classified admissions based on the presence (n = 51) or absence (n = 105) of anemia prior to treatment. They found that hemoglobin improved by 0.7 g/dl ($p < 0.001$) and 0.2 g/dl ($p = 0.047$) when anemia was present and not present, respectively, at admission. Hemoglobin responses in both groups were unrelated to prior use of an oral iron supplement. They concluded that intravenous antibiotics improved hemoglobin during exacerbation by increasing iron availability, which in turn reflected lower activity of interleukin-6 (IL-6) and hepcidin-25. Indeed, IL-6 stimulates hepatic production of hepcidin-25, a hormone that induces hypoferremia by restricting duodenal iron absorption [2] and causing mononuclear cells to retain iron [3].

I believe that in order to accurately interpret the findings of Kathiresan et al. [1], the authors should specify the hemoglobin cutoffs used to distinguish anemia and clarify whether patients with repeated exacerbations were included in the analysis. In a cross-sectional study [4], our group has shown that 14 adult CF patients with median plasma iron and hemoglobin concentrations of 3.6 μmol/l and 11.3 g/dl, respectively, had significantly worse lung function and lower body mass index than 25 CF patients of similar age with respective median plasma iron and hemoglobin levels of 9.0 μmol/l and 13.5 g/dl. Based on these observations, we concluded that anemia and hypoferremia are emblematic of disease severity.

It is reasonable to speculate that severely anemic and hypoferremic CF patients are not only more likely to have exacerbations but also more likely to respond to antibiotics with an increase in hemoglobin. If such patients were repeatedly admitted, and hence, constituted a high percentage of consecutive admissions analyzed by Kathiresan et al. [1], their findings may apply to specific patients. I cannot find published data which relates hospitalization risk to anemia severity. In a retrospective analysis of risk factors for oral or intravenous antibiotic treatment in 55 unique adults treated at our CF center, we determined that a one-time hemoglobin measurement ≤12.9 g/dl was associated with higher risk of subsequent treatment (HR = 1.63, 95% CI 0.94–2.86, $p = 0.049$) (Fig. 1). It would be interesting to know if patients who were defined as anemic and considered more than once in their series had hemoglobin levels <12.9 g/dl at the time of admission.

In our recent description of iron homeostasis during CF exacerbation [5], we reported that IV antibiotics increased median serum iron level by 2.42 μmol/l and reduced median serum IL-6 and hepcidin-25 concentrations by 12.1 pg/ml and 37.5, respectively, among 12 unique adults who were hospitalized for exacerbation ($p < 0.05$ for all comparisons). Thus, we confirmed the aforementioned postulate of Kathiresan et al. [1], but we did not detect a statistically-significant difference in hemoglobin concentration after 12 days of treatment. Aggressive phlebotomy did not explain this finding. It remains possible that the increase in serum iron was insufficient for erythropoiesis, that erythropoiesis was still blunted by inflammation, or that the equivocal hemoglobin difference represented type II error. The critical implications of our data and those of Kathiresan et al. [1] are that antibiotics dramatically influence circulatory biomarkers of iron status and may have a positive effect on hemoglobin concentration in this patient population.

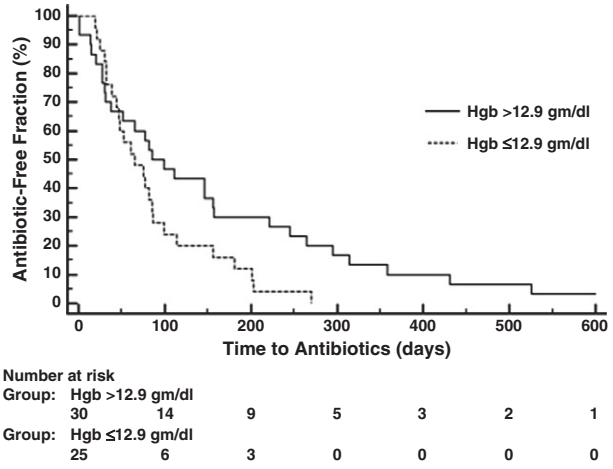

Fig. 1. Kaplan-Meier analysis showing that CF patients with hemoglobin ≤ 12.9 g/dl were more likely than those with higher values to receive to antibiotics.

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References

[1] Kathiresan B, Waine D, Derry D. The effect of intravenous antibiotics on anaemia in cystic fibrosis. J Cyst Fibros 2013;12(6):828–9.
[2] Ganz T, Nemeth E. Hepcidin and disorders of iron metabolism. Annu Rev Med 2011;62:347–60.
[3] Theurl I, Theurl M, Seifert M, Mair S, Nairz M, Rumpold H, et al. Autocrine formation of hepcidin induces iron retention in human monocytes. Blood 2008;111(4):2392–9.
[4] Gifford AH, Miller SD, Jackson BP, Hampton TH, O'Toole GA, Stanton BA, et al. Iron and CF-related anemia: expanding clinical and biochemical relationships. Pediatr Pulmonol 2011;46(2):160–5.
[5] Gifford AH, Moulton LA, Dorman DB, Olbina G, Westerman M, Parker HW, et al. Iron homeostasis during cystic fibrosis pulmonary exacerbation. Clin Transl Sci 2012;5(4):368–73.

A.H. Gifford
Pulmonary and Critical Care Medicine, Dartmouth-Hitchcock Medical Center, NH, Lebanon
Section of Pulmonary and Critical Care Medicine, 5C, Dartmouth-Hitchcock Medical Center, One Medical Center Drive, NH 03756-1000, Lebanon. Tel.: +961 603 650 5533; fax: +961 603 650 0580.
E-mail address: giffora@hitchcock.org.

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